

OFFICE OF NAVAL RESEARCH

Contract N00014-92-J-1433

R & T Code 4132038

Technical Report No. 27

The Synthesis of ROMP Homopolymers and Multi-Block Copolymers Containing Sugars

by



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submitted

to

J. Am. Chem. Soc.

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June 14, 1995

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19950626 046

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. AGENCY USE ONLY (Leave blank)

2. REPORT DATE

6-14-95

3. REPORT TYPE AND DATES COVERED

Technical Report

4. TITLE AND SUBTITLE

The Synthesis of ROMP Homopolymers and Multi-Block Copolymers Containing Sugars

5. FUNDING NUMBERS

G- N00014-92-J-1433
R&T Code 4132038

6. AUTHOR(S)

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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Cambridge, MA 02139

8. PERFORMING ORGANIZATION
REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

Department of the Navy
Office of Naval Research
800 North Quincy Street
Arlington, VA 22217-5000

10. SPONSORING/MONITORING
AGENCY REPORT NUMBER

27

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION AVAILABILITY STATEMENT

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12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 words)

Ring-opened homopolymers of 1,2:3,4-di-O-isopropylidene- α -D-galactopyranos-6-O-yl-5-norbornene-2-carboxylate (1) and bis(1,2:3,4-di-O-isopropylidene- α -D-galactopyranos-6-O-yl)-5-norbornene-2,3-dicarboxylate (2) were prepared in toluene in a living manner using $\text{Mo}(\text{CHCMe}_2\text{Ph})(\text{N}-2,6\text{-i-Pr}_2\text{C}_6\text{H}_3)(\text{O}-t\text{-Bu})_2$ as the initiator. These homopolymers have low PDI's (as low as 1.06) and molecular weights that are proportional to the number of monomers added. Various di-, tri-, and tetra-block copolymers containing 1, 2, methyltetracyclododecene (MTD, 3), or trans-2,3-bis(trimethylsilyloxymethyl)-norborn-5-ene (4) could also be prepared and were found to have polydispersities as low as 1.03. The sugars are easily deprotected to give sugar-derivatized, water-soluble polymers.

14. SUBJECT TERMS

15. NUMBER OF PAGES

16. PRICE CODE

17. SECURITY CLASSIFICATION
OF REPORT

Unclassified

18. SECURITY CLASSIFICATION
OF THIS PAGE

Unclassified

19. SECURITY CLASSIFICATION
OF ABSTRACT

Unclassified

20. LIMITATION OF ABSTRACT

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The Synthesis of ROMP Homopolymers and Multi-Block Copolymers Containing Sugars

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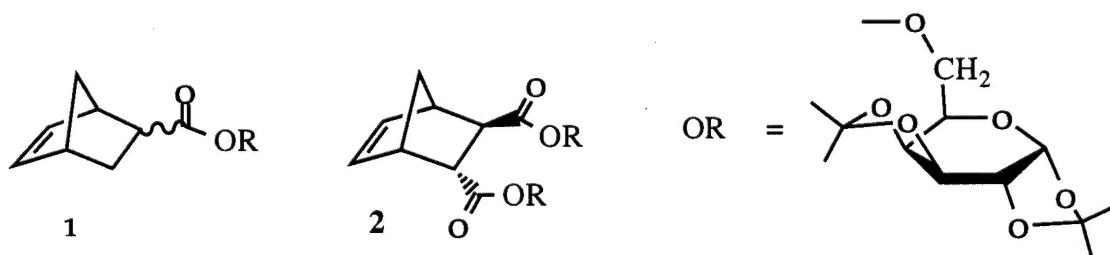
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Abstract

Ring-opened homopolymers of 1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranos-6-*O*-yl-5-norbornene-2-carboxylate (**1**) and bis(1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranos-6-*O*-yl)-5-norbornene-2,3-dicarboxylate (**2**) were prepared in toluene in a living manner using $\text{Mo}(\text{CHCMe}_2\text{Ph})(\text{N}-2,6\text{-i-Pr}_2\text{C}_6\text{H}_3)(\text{O}-t\text{-Bu})_2$ as the initiator. These homopolymers have narrow molecular weight distributions (PDI's as low as 1.06) and molecular weights that are proportional to the number of monomers added. Various di-, tri-, and tetra-block copolymers containing **1**, **2**, methyltetracyclododecene (MTD, **3**), or trans-2,3-bis(trimethylsilyloxymethyl)-norborn-5-ene (**4**) could also be prepared and were found to have polydispersities as low as 1.03. The cyclic acetal in polymers containing **1** or **2** can be cleaved using trifluoroacetic acid in water in 15 minutes at room temperature to afford the corresponding sugar-derivatized, water-soluble polymers.

Methods for synthesizing carbohydrate-modified polymers have been sought in recent years in view of the possibility that such polymers could mimic natural carbohydrates in binding to cell surfaces.^{1,2} The vast majority of such polymers have been prepared by traditional free radical polymerizations of acrylamide derivatives,³⁻⁷ one recent exception being the preparation of cell agglutination inhibitors by aqueous Ru catalyzed ROMP (Ring-Opening Metathesis Polymerization) of glucose-derivatized 7-oxynorbornene.⁸ None of these processes is living. Living polymerization techniques for preparing such polymers could have distinct advantages since the molecular weight distribution can be as narrow as possible, block copolymers can be prepared (e.g., hydrophobic/hydrophilic), and functional end groups could be attached to one or both ends of the polymer. Molybdenum alkylidene complexes of the type $\text{Mo}(\text{CHR}')(\text{NAr})(\text{OR})_2$ ($\text{Ar} = 2,6\text{-i-Pr}_2\text{C}_6\text{H}_3$, $\text{OR} = \text{t-Bu}$, $\text{CMe}(\text{CF}_3)_2$, etc.; $\text{R}' = \text{CMe}_3$ or CMe_2Ph)⁹ have been shown to be useful initiators for the living ROMP of cyclic olefins, especially norbornenes and disubstituted norbornadienes,^{10,11} in part since a wide variety of non-protic functionalities are tolerated by this type of catalyst and secondary metathesis is often slow. The ability to prepare highly tactic all cis or all trans ROMP polymers^{12,13} adds another dimension to the method, as the resulting polymers could have specific secondary or tertiary structures. We report here the first results of our efforts to synthesize sugar-derivatized polymers by Mo-catalyzed living ROMP using $\text{Mo}(\text{CHCMe}_2\text{Ph})(\text{NAr})(\text{O-t-Bu})_2$ as the initiator.

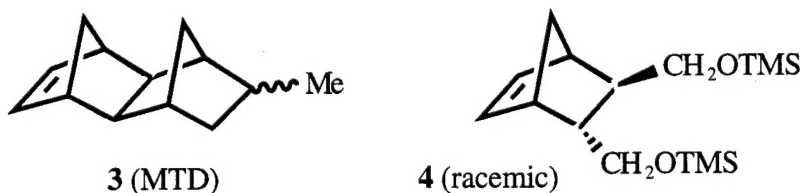
Monomers **1** (*endo,exo* mixture), and **2** (*trans*- racemic) were prepared by adding 1,2:3,4-di-O-isopropylidene- α -D-galactopyranose to the corresponding norbornene carbonyl chlorides.¹⁴ It is important to note that both **1** and **2** can be purified by multiple recrystallizations from mixtures



of ether and pentane, as monomer purity is crucially important for successful living polymerizations with well-defined Mo catalysts.¹¹ Monomers **1** and **2** were polymerized in toluene by adding *n* equivalents to $\text{Mo}(\text{CHCMe}_2\text{Ph})(\text{NAr})(\text{O}-t\text{-Bu})_2$ and the polymers were cleaved from the metal with benzaldehyde.¹⁵ Proton NMR spectra of poly(**1**) and poly(**2**) showed the expected broad olefinic resonances between 5.1 and 5.5 ppm and relatively sharp resonances for the sugar residue. Poly(**1**) and poly(**2**) almost certainly do not have regular structures, as (in part) **1** does not contain a plane of symmetry and **2** is racemic. The PDI of poly(**1**) (Table 1) is significantly lower than that of poly(**2**) and the ratio of the M_n found by light scattering to the M_n calculated on the basis of the amount of initiator employed is also smaller for poly(**1**) than for poly(**2**).¹⁶ Reaction times significantly greater than those listed in Table 1 led to significantly higher PDI's. The approximately linear relationship between the M_n (found) and the number of equivalents of monomer added suggests that this polymerization is living, as has been demonstrated for many norbornenes that contain a variety of non-protic functionalities.¹¹ **2** appears to be polymerized more slowly than **1**, as one might expect on the basis of steric factors.

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Methyltetracyclododecene (MTD, **3**) and trans-2,3-bis(trimethylsilyloxymethyl)norborn-5-ene (**4**) were selected as comonomers in block copolymer synthesis, since MTD has been used before to synthesize block copolymers (and it has a relatively high T_g),¹⁸⁻²⁰ and since **4** hydrolyzes readily to the diol. Poly(**4**) prepared using $\text{Mo}(\text{CHCMe}_2\text{Ph})(\text{NAr})(\text{O}-t\text{-Bu})_2$ as the



initiator had a low polydispersity (1.10; Table 1) and a low value for M_n (found)/ M_n (calcd) (1.32), as expected. Di-, tri-, and tetrablock copolymers containing **1** or/and **2** were prepared by adding 25 or 50 equivalents of the monomers sequentially to $\text{Mo}(\text{CHCMe}_2\text{Ph})(\text{NAr})(\text{O}-t\text{-Bu})_2$ (Table 1) and isolated in a manner analogous to that used to isolate the homopolymers.¹⁵ Changing the

order of addition of monomers (e.g., 3/4/2 vs. 2/4/3) had no significant consequence on either $M_n(f)/M_n(c)$ or PDI. The appearance of an increasingly intense high molecular weight shoulder for multiblock copolymers is consistent with observations noted above concerning degradation of homopolymers after several hours under the reaction conditions employed.

The sugars in the polymers were deprotected using a 9:1 mixture of trifluoroacetic acid and water.²¹ (Hydrolysis of cyclic acetals of ketoses by acetic acid, oxalic acid, ion exchange resin, or mixtures of trifluoroacetic acid and water are well-known.^{22,23}) The deprotected polymers were isolated by pouring the mixture into THF at -30 °C. NMR spectra of the deprotected polymers in dmf-d₆ showed no resonances for the cyclic acetals, while IR spectra showed a broad absorption band at ~3415 cm⁻¹ characteristic of sugar hydroxyls but no absorptions ascribable to carboxylic acids. The deprotected homopolymers and block copolymers are soluble to varying degrees in dimethylsulfoxide, dimethylformamide, and water. They are slightly soluble in methanol and THF, and insoluble in toluene, hexane, and pentane.

The techniques described here involve *nonaqueous* polymerization methods. *Aqueous* ROMP methods^{8,24-26} are not *required*, as protected sugars are widely available and protection is required in order to prepare a ROMP monomer even for aqueous polymerization.⁸ It is also important to note that the t-butoxide initiator is only one of several that have been employed successfully in living ROMP reactions in which aprotic functionalities are present, and that all *cis*,isotactic and all *trans*,syndiotactic polymers have been prepared from achiral or enantiomerically pure norbornenes or norbornadienes.^{12,13} Future efforts will be aimed at determining what other initiators and monomers can be employed, what end groups can be added, and whether a regular secondary structure can be induced in a polymer that has a specific primary structure (e.g., *cis*,isotactic).

Acknowledgements. R.R.S. thanks the Navy for supporting research on ring opening metathesis polymerization and K.N. thanks the Sumitomo Chemical Co., Ltd. for support.

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- (14) For example, a solution of 2-norbornene-5-carboxylic acid chloride (1.79 g, 11.4 mmol) in ether (20 mL) was added dropwise over a period of 1 h into a solution of 1,2:3,4-di- α -O-isopropylidene-D-galactopyranose (3.0 g, 11.5 mmol) dissolved in ether (50 mL) and triethylamine (1.28 g, 12.68 mmol) at -50°C under a nitrogen atmosphere. The reaction mixture was stirred for 10 h and filtered. The ether was removed from the filtrate and the residue was dissolved in a minimum amount of THF (3-5 mL) and the solution was added to vigorously stirred ice water (800 mL) to give white granules. The white solid was filtered off, dried *in vacuo* overnight, and recrystallized in a drybox under dinitrogen from chilled mixtures of ether and pentane at -30°C; yield 55%.

- (15) For example, a solution of $\text{Mo}(\text{CHCMe}_2\text{Ph})(\text{N}-2,6\text{-i-Pr}_2\text{C}_6\text{H}_3)(\text{O}-t\text{-Bu})_2$ (2-7 mg in 0.3 - 1.0 mL of toluene) was added in one portion to a rapidly stirred solution of monomer in toluene (2-5 mL) at room temperature. After monomer was consumed the polymerization was quenched by adding benzaldehyde (~10 mg). After 1 h the solvents were removed *in vacuo*, the resulting solid was dissolved in minimal THF (~2 mL), and the solution was poured into vigorously stirred cold water (~80 mL) to give white to pale yellow precipitates that were collected by filtration and dried *in vacuo*. Yields were ~95% or greater in all cases.
- (16) $M_n(\text{f})/M_n(\text{c})$ ratios significantly greater than 1 could result from some deactivation of the initiator or propagating alkylidenes by traces of water or other protic impurities, or by traces of oxygen, in spite of the rigorous experimental techniques. The reasons for $M_n(\text{f})/M_n(\text{c})$ ratios as high as 2.7 in these systems is not yet known.
- (17) For example, a reaction involving 100 equivalents of **1** was complete in 1 h, whereas 22% of 50 equiv of **2** remained (by proton NMR) after 1 hour in an analogous reaction.
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- (21) For example, the polymer (~150 mg) was added to a stirred mixture of $\text{CF}_3\text{CO}_2\text{H}$ and water (9/1, v/v; ~ 1 mL). After 15 minutes at room temperature the solution was poured into 15 mL of vigorously stirred THF that had been cooled to ca. -30 °C. The white precipitate was filtered off, washed with hexane, and dried *in vacuo*. Yields were > 90% in all cases. The polymers could be purified further by pouring a DMF solution into chilled (ca. -30 °C) toluene.
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Table 1. Protected Sugar-Derivatized Polymers Prepared by Ring-Opening Metathesis

Polymerization using $\text{Mo}(\text{CHCMe}_2\text{Ph})(\text{NAr})(\text{O}-t\text{-Bu})_2$ as the Initiator.

Monomer(s) ^a	Equiv ^b	time (h) ^b	$10^{-4}M_n(\text{c})^c$	$10^{-4}M_n(\text{f})^d$	$M_n(\text{f})/M_n(\text{c})$	PDI
1	20	1	0.76	1.47	1.93	1.06
1	30	1	1.14	1.67	1.46	1.06
1	50	1	1.90	2.77	1.45	1.06
1	100	1	3.80	6.31	1.66	1.10
2 ^e	20	1	1.33	3.27	2.45	1.25
2 ^e	30	1.5	2.00	5.33	2.67	1.21
4	50	1	1.49	1.96	1.32	1.10
3/1	25/25	1/1	1.39	1.68	1.21	1.03
3/1	50/50	1/1	2.77	4.89	1.77	1.18
3/2	25/25	1/1	2.10	2.64	1.26	1.17
4/1	25/25	1/1	1.70	3.75	2.21	1.08
3/1/2 ^e	25/25/25	1/1/1.5	3.05	4.27	1.40	1.05
3/4/1	50/25/25	1/1/1	2.57	4.30	1.67	1.09
3/4/1	50/25/50	1/1/1	3.52	5.51	1.56	1.17
3/4/2 ^e	50/25/25	1/1/1.5	3.28	7.66	2.33	1.16
2/4/3 ^e	25/25/50	1/1/1	3.28	7.31	2.23	1.13
3/4/1/2	50/25/25/25	1/1/1/1.5	4.24	10.75	2.54	1.05
				10.39	2.45	1.08
1/2/1/2	25/25/25/25	1/1.5/1/1.5	5.24	11.26	2.15	1.03

^a The sequence in which monomers were added is that shown in the first column. ^b Equivalents and times correlate with the sequence shown in the first column. ^c Calculated on the basis of the monomer/catalyst ratio. ^d Found by light scattering at 690 nm in dichloromethane. ^e A small high MW shoulder was observed in the GPC trace.